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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,865	10/15/2001	J Kevin Donahue	001107.00449	3724

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EXAMINER
KATCHEVES, KONSTANTINA T

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,865	DONAHUE ET AL.	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 70-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,70-83,85-91,93-99,102-105 and 108-111* is/are rejected.

7)☒ Claim(s) *84,92,100,101,106 and 107* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~1/5/05~~. 2/2/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 70-111 are pending in the present application.

Response to Arguments

Claims 1,70-83, 85-91, 93-99, 102-105, and 108-111 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *ex vivo* methods of nucleic acid delivery and direct injection of nucleic acids, does not reasonably provide enablement for all *in vivo* methods of delivery.

Applicant's arguments filed 05 January 2005 have been fully considered but they are not persuasive.

Applicant traverses the rejection under 35 U.S.C. 112, first paragraph argueing that the examiner has not met her burden in showing that *in vivo* perfusion to deliver nucleic acids to desired tissues is not enabled. Applicant provides a declaration by Dr. Kevin Donohue and exhibits in support of the assertion that *in vivo* perfusion to desired tissues is enabled. Applicant's arguments are noted; however not persuasive as to the breadth of the claims.

The declaration by Dr. Donohue states that "[g]ene transfer and expression was detected in 45% of the cells of the atrioventricular (AV) node." In the article by Donohue et al. (Nature Medicine Vol.6 no.12 2000), more detail is available regarding this assertion. The method of delivery used to provide the vector to the desired cells was *in vivo* perfusion. The right coronary artery was catheterized via the right carotid artery. See Donohue et al. p.1397. The subjects were also provided with oral sildenafil and VEGF, nitroglycerin and virus contain solutions were infused into the AV nodal branch of the right coronary artery.

The results discussed in the article and in the declaration by Dr. Donohue and the article, show that 45% of the cells in the AV node show gene transfer by measured β-gal activity. The article discusses that "β-gal activity was evident in gross specimens from liver, kidneys and ovaries. No staining was evident in lungs or skeletal muscle. Microscopic sections revealed β-gal activity, but in less than 1% of the cells in these organs." The results discussed actually punctuate the problem of gene delivery. The site of the most direct administration of the viral solution showed the highest delivery of the viral transgene. The distal sites, i.e. liver, kidneys and ovaries, showed significantly decreased transgene activity in gross specimens, and sites like lungs and skeletal muscle showed activity only in microscopic sections in less than 1% of those cells. The article also does not show additional western blot data for the cells in the liver, kidney, ovary, lung or skeletal muscle cells as it does for the cardiac myocytes. The data also fails to show long term expression of the transgene. This data supports the questions raised by the examiner in previous office actions: can the transgene be specifically delivered; can the transgene achieve long-term stable expression; can the transgene reach enough of the target cells; and can the genes function properly for a significant period of time. The primary goal of the study was to "overcome the problem of vector delivery to the myocardium using minimally invasive techniques." See Donohue et al. page 1397, column 1. Donohue et al. never sought to address the At best, based on the data provided, the data shown support that Applicant is enable for *in vivo* perfusion into cardiac tissue, in addition to the *ex vivo* and direct injection methods previously discussed. Therefore, the invention is not enabled for the full scope claims.

Allowable Subject Matter

Claims 84, 92, 100, 101, 106, 107 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (571) 272-0768. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 7:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Konstantina Katcheves
Examiner
Art Unit 1636

JAMES KETTER
PRIMARY EXAMINER